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A one-year-survey of Carbapenemase-producing Klebsiella pneumoniae in Italy: Beyond the ICU

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Sir,

The spread of carbapenemase-producing *Klebsiella pneumoniae* (KPC-Kp) has become a worldwide problem in recent years with a reported fatality rate from 22% to 72% [1]. In Europe, outbreaks of KPC-Kp have been reported in several countries, but data from the EARS-NET surveillance system showed that, until 2009, the proportion of KPC-Kp remained stable in most countries except Greece and Italy where an increase has been reported from 1-2% in 2006-2009 to 15.2% in 2010 and 27% in 2011 [1]. This trend has recently been confirmed by the Micronet sentinel surveillance network and a recent countrywide cross-sectional survey, outlining the epidemic dissemination in Italy of carbapenem-resistant Enterobacteriaceae (CRE), mostly related to the clonal diffusion of type A KPC-Kp of clonal complex 258 [3-4]. More recently, data from Italian local surveillance systems revealed a persistent condition of KPC-Kp endemicity in hospitals from the North area [5]. In this work, we report results of a one-year-based nosocomial survey of KPC in Italy North-West Italy, covering the metropolitan area of Turin (2,297,917 inhabitants with 5 tertiary referral centers). Aims were to focus on KPC epidemiology in hospital wards as well as antibiotic susceptibility patterns in the year 2012.

The regional surveillance program for infection control In Piedmont, Italy North-West depends from the national and the EARS-NET surveillance systems. It is organized as a network involving Public Health Infection Control Units from regional hospitals with a central coordination board. Data collection is yearly made and involve 29 regional Units covering all the area (4,374,000 inhabitants, 620,917 hospital admissions and 4,314,245 hospital days/year) including 8 tertiary referral and 21 secondary care centres, whose mandatory task on a year-base is to report KP and KPC-Kp clinical isolates from any sample (e.g. urine, blood, sputum, tracheal aspirate, bronchoalevolar lavage, injury swab, abdominal drainage fluid) to investigate the local KPC-Kp epidemiology. The data-set referred to the year 2012 was analysed including only non-duplicate clinical isolates and, for each isolate, site of sampling, antibiotic susceptibility pattern and hospital ward. Data referring to KPC-Kp screening from rectal swabs were not included.

Participating laboratories were asked to provide full information on the methods used for KPC-Kp identification (e.g. automated systems) and antibiotic susceptibility. KPC-kp showing a pattern of multiresistance (MIC for meropenem >0.5 mg/l) were evaluated for carbapenemase production by meropenem plus EDTA and meropenem plus phenylboronic acid using the disk diffusion method. MICs to Colistin, Tigecycline and Gentamicin were confermed with the E-test (bioMérieux, Marcy l'Etoile, France).

There were 8,179 Kp isolates from different samples and 1,433 isolates were confirmed as KPC-Kp (17.5%). Tertiary hospitals accounted for the highest KPC-Kp absolute number and the highest rate; being in 5/8 significantly higher than the average count (49; 13.4%). According to hospital admissions, average KPC-Kp incidence was 1.9 per 1,000, with peaks in 7/8 tertiary hospitals. Overall, there was a reduction of KPC-Kp incidence per hospital admissions compared to 2011 (average: 3/1,000), which was important in three tertiary centres (ID# 26T, 23T and 24T).

The majority of KPC-Kp were isolated from urine (50%), respiratory samples (22%) and blood (12%). As many as 31% of KPC-Kp were isolated from patients admitted to medical wards followed by those in ICU (15%), emergency department (14%), surgical

wards (13%,) and long-term facilities (10%). Sample distribution was different according to wards of admission (**Figure 1)**: in medical wards, emergency departments and long term facilities the majority of KPC-Kp were urinary (56%; 85%; 84%; respectively), whilst in ICU there were more isolates from respiratory tract (56%) and blood (16%). Importantly, KPC-Kp positive blood cultures were found at a similar rate in ICU and medical wards (16%).

Antibiotic susceptibility in secondary and tertiary care centres, respectively, ranged from 75%-100% vs. 67%-90% for colistin, 10%-71% vs. 6%-57% for tigecycline, and 50%-100% vs. 30%-55% for gentamicin. Colistin and tigecycline were tested in only 71% and 43% of laboratories, respectively, mainly in tertiary hospitals (**Table 1**).

A rapid dissemination of KPC-Kp has been reported in Italy since 2010 [2] and confirmed in recently published cross-sectional surveys, challenging the health care system for infection control and prevention procedures. This is the first survey in the North-West of Italy, covering a wide geographical area (4,374,000 inhabitants) and confirming KPC-Kp epidemic diffusion. Our results are in line with those reported from national surveillance system (11.9%) and other recent local report (19.4%) [2-3]. Our results showed that the majority of KPC-Kp were isolated in the year 2012 from patients admitted to tertiary referral centres, even if KPC-Kp incidence decreased compared to the year 2011 in these type of hospitals. Tertiary hospitals accounted for the highest absolute number and rate of KPC, but our data definitively show that the KPC-Kp diffusion is also affecting secondary care hospitals, being the incidence of KPC-Kp above the regional average in one third of them, underscoring that these data should be considered when planning infection control strategies. Moreover, our data highlighted a new trend in KPC-Kp infections, affecting more medical wards with a high number of urinary colonization in this setting compared to ICU, where KPC-Kps were isolated mostly from respiratory airways and blood, suggesting that KPC-Kp is no longer a major issue for critically ill patients [11].

In conclusion, encouraging results of this survey confirm a decreasing trend in KPC-Kp mainly in tertiary referral hospitals. However, KPC-Kp is becoming a challenge also for secondary care hospitals as well as medical wards, confirming that continuous surveillance is important and that implementation of infection control measures at both local and regional level is a key issue for success in this advanced phase of the epidemics. Nowadays, the analysis of susceptibility to colistin and tigecycline should be mandatory in laboratory procedures.

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Table 1. Percentage of susceptibility to colistin, tigecycline and gentamycin in partecipant centers.

Hospital ID	Colistin Susceptibility (%)	Tigecyclin Susceptibility (%)	Gentamycin Susceptibility (%)
1	100	NA	50
3	82,3	NA	30
4	100	NA	50
5	75	71	50
6	94,6	NA	64,7
8	91,7	6,8	30,6
12	NA	NA	52,5
13	90	NA	58,5
14	51,8	92,3	33,3
15	64,3	41,7	35,7
16	95	100	70
18	NA	NA	100
19	100	100	83,8
19	NA	NA	53,6
20	84,6	NA	54
22	100	100	14
25	NA	NA	20
17T	75	NA	62,5
23T	95	NA	49
24T	74,2	57,2	54,5
26T	67	NA	20
27T	NA	96,3	38
28T	90	12,5	41,7
2T	98,7	5,5	55,8
9T	87,8	NA	46,3

Susceptibility data were available for 25 out of 28 hospital centers. T= tertiary care centers; NA= not applicable